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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Terri L. Butler et al.
Title: COMPOSITIONS AND METHODS FOR IMPROVING CARDIOVASCULAR FUNCTION

Docket No.:	BP028US1	Serial No.: 10/692,338
Filed:	October 23, 2003	Due date:
Examiner:	Traviss C. McIntosh IIII	Group Art Unit: 1623

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Examiner McIntosh:

I am pleased to inform you that the European Patent Application, corresponding to the above referenced US Application has been allowed, subject to minor editing. I am enclosing the European claims and some supplemental information, which may be helpful to you in examining this case.

Dr. John St. Cyr, an inventor on this application, and I would welcome an interview, in person or by phone, if you feel such an interview would assist you in examining the case.

By Kathleen R. Terry
Kathleen R. Terry
Reg. No. 31884

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Certificate under 37 CFR 1.1 0: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service Express Mail, in an envelope with first class postage,addressed to: Commissioner for Patents, Box 1450, Alexandria, VA 22313-1450 on this 21st day of April, 2006.

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BY FACSIMILE

12th April 2006

CONFIRMATION OF FAX

Kay Terry
Bioenergy, Inc.
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USA

Dear Kay

Re: European Patent Application No. 01 956170.3
(Publication No. 1 313 488) derived from
PCT Patent Application No. PCT/US01/41448
(Publication No. WO02/09727)
(Filed 27th July 2001) claiming priority from
US Application No. 60/221526 (Filed 28th July 2000) and
US Application No. 09/677639 (Filed 3rd October 2000) and
US Application No. 60/302220 (Filed 29th June 2001)
Applicant: Bioenergy, Inc.
Inventors: Butler, T.L.; St. Cyr, J.; Johnson, C.A.
Compostions and Methods for Improving Cardiovascular Function
Case: BEN,374.028-PCT-EP (374.028-PCT-EP)

By Fax

I enclose an official letter which has been issued by the European Patent Office in connection with this application.

As you will see, the Examiner has now indicated that the claims are allowable and has simply requested that we bring the description in to conformity with the amended claims.

I assure that you would like Paul to take care of this but would appreciate your confirmation.

We have been given until 6th June 2006 in which to reply to the official action although this period will be automatically extendible by two months on our request.

We look forward to receiving your instructions well before the due date.

Best wishes.

Yours sincerely

Brian Lucas/zt
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14th December 2005

The European Patent Office
Erhardtstrasse 27
D-80298 Munich
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Dear Sirs

Re: European Patent Application No. 01 956170.3
(Publication No. 1 313 488) derived from
PCT Patent Application No. PCT/US01/41448
(Publication No. WO02/09727)
(Filed 27th July 2001) claiming priority from
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We write in response to the supplementary European Search Report dated 13th October 2005.

With reference to the Pliml et al citation, Dr Pliml has tried for many years to find a way to use Ribose in various conditions discussed in a declaration by Dr John St. Cyr which was filed with our letter of 18th August 2005. The original work by Doctors John Foker and John St. Cyr was one of the first attempts to study Ribose in an intact mammal. In that study, healthy dogs weighing about 25kg were subjected to 20 minute cardiac cross-clamping. After this induced global ischemia, ATP levels were very low (about 50% of pre-operative levels) and Ribose was given intravenously to enhance recovery. The dosage of Ribose was about 17g per day with 100% bioavailability. Following the teachings of Dr Foker and Dr Zimmer, Dr Pliml's study of 20 men with ischemic heart disease used correspondingly high doses of oral ribose, that is 60g a day in four doses. A base-line treadmill exercise was performed. After three days of Ribose administration, treadmill exercise time to angina was improved. The dosage was not continued chronically to determine whether the effect would persist or even provide further improvement. It is the applicant's experience that doses over 8g cause unacceptable gastro-intestinal distress and therefore patient non-compliance would be a barrier to chronic use. In addition it should be noted that Dr Pliml co-administered glucose with

co-administered glucose as defined in the claims filed on 18th August 2005 would be effective and could be administered chronically.

JP-A-02286620 describes the use of a polysaccharide, including a Ribose polysaccharide found in green tea. No further description of this polysaccharide is provided.

The JA St. Cyr reference is believed to have provided the basis of the subsequent work of Dr Pliml. The disclosure of that reference adds nothing to the disclosure of Pliml et al.

US 6159942 is an earlier patent filed by the present applicant. It discloses the use of Ribose in healthy people, not people undergoing cardiac rehabilitation. Example 5 shows a patient with coronary artery disease who was considered to be healthy following coronary artery bypass grafting. He had no angina even on treadmill testing. Example 6 shows a person recovering from a severe bacterial infection. He is described as recovered, with no overt disease. It would not be known from this study whether cardiac patients requiring rehabilitation could benefit from low doses of oral ribose.

US Patent 6218336 is a further patent filed by the present applicant. It discloses an acute study for uncovering hibernating myocardium. Example 5, considered by the Search Examiner to be relevant, is a short-term 3 day trial of Ribose at does of about 13g per administration which is a relatively high dose. Example 6 discloses potential benefits of co-administering a vasodilator with Ribose, but is silent about the dosage to be administered.

Loscalzo is a review of the state of knowledge in 1995 concerning nitric oxide which is an ubiquitous cell effector. No mention is made of ATP re-synthesis, or of the effect of Ribose on Nitric Oxide generation.

The Zimmer paper concerns intact rats who were subjected to regional cardiac ischemia. Recovery was found to be enhanced by very high levels (200mg/kg/hour) of intravenously administered Ribose. Applicants point out that these were young healthy animals subjected to an acute ischemic event, whereas cardiac patients have a chronic condition that develops over time and requires chronic therapy. This point is also made in the discussion of the Pliml paper above.

The Mahoney paper reports that Ribose cannot be used as a sole energy source in the isolated working rat heart. These findings say nothing about low does of ribose supplemented with the energy sources of a normal diet in intact mammals.

The Applicants wish the Examination to proceed on the basis of claims 1 to 11 filed with our letter of 18th August 2005. Claim 1 specifies that D-Ribose is used in the manufacture of a medicament to be administered as a unit dosage of 2-8g of Ribose 2 or 3 times per day for treatment of coronary artery disease and congestive heart failure on a maintenance basis and without abdominal distress and diarrhoea. It is believed that the subject matter of claim 1 is novel and inventive having regard to each of the references found in the Search Report, none of which discloses a dosage regime for Ribose which can be taken by patients with artery disease or heart failure over an extended period.

May we remind you that the present application is the subject of a request for accelerated Search and Examination under the PACE program. We await the results of further examination of this application.

Would you please return the attached copy of this letter to acknowledge safe receipt hereof.

Yours faithfully

Paul Cole/kt
Chartered Patent Agent
European Patent Attorney
Authorised Representative